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Use and Environmental Occurrence of Antibiotics in Freestall Dairy Farms with Manured Forage Fields

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Environmental releases of antibiotics from concentrated animal feeding operations (CAFOs) are of increasing regulatory concern. This study investigates the use and occurrence of antibiotics in dairy CAFOs and their potential transport into first-encountered groundwater. On two dairies we conducted four seasonal sampling campaigns, each across 13 animal production and waste management systems and associated environmental pathways: application to animals, excretion to surfaces, manure collection systems, soils, and shallow groundwater. Concentrations of antibiotics were determined using on line solid phase extraction (OLSPE) and liquid chromatography-tandem mass spectrometry (LC/MS/MS) with electrospray ionization (ESI) for water samples, and accelerated solvent extraction (ASE) LC/MS/MS with ESI for solid samples. A variety of antibiotics were applied at both farms leading to antibiotics excretion of several hundred grams per farm per day. Sulfonamides, tetracyclines, and their epimers/isomers, and lincomycin were most frequently detected. Yet, despite decades of use, antibiotic occurrence appeared constrained to within farm boundaries. The most frequent antibiotic detections were associated with lagoons, hospital pens, and calf hutches. When detected below ground, tetracyclines were mainly found in soils, whereas sulfonamides were found in shallow groundwater reflecting key differences in their physicochemical properties. In manure lagoons, 10 compounds were detected including tetracyclines and trimethoprim. Of these 10, sulfadimethoxine, sulfamethazine, and lincomycin were found in shallow groundwater directly downgradient from the lagoons. Antibiotics were sporadically detected in field surface samples on fields with manure applications, but not in underlying sandy soils. Sulfadimethoxine and sulfamethazine were detected in shallow groundwater near field flood irrigation gates, but at highly attenuated levels.

Introduction

Pharmaceuticals of both human and veterinary origins have been widely detected in various environmental matrices including surface water, groundwater, soils, and sediments (*1, 2*). The use of veterinary antibiotics in concentrated animal feeding operations (CAFOs) is a growing concern as a significant source of contamination (*3*). Antibiotics are used in livestock production to prevent and treat diseases, promote growth, and improve productivity (*4*). In the U.S., 12.6 thousand metric tons of antibiotics were sold for animal use in 2007, 13% of which were administered to promote growth and efficiency (*5*). Antibiotics and their metabolites are excreted in feces and urine, and escape containment during normal waste management operation and surface runoff (*6*). Once antibiotics are released from CAFOs, they may affect terrestrial and aquatic organisms (*7–9*) and may lead to the development of antibiotic-resistant strains of microorganisms (*10–12*).

California is the largest U.S. producer of milk and cheese with 1.8 million milking cows, making freestall dairies the state's most prevalent CAFO industry. Most of California's dairies are located in the San Joaquin Valley (*13*), a topographically flat region overlying predominantly alluvial and fluvial unconsolidated sediments with some areas of shallow water table, which are particularly vulnerable to groundwater contamination. Little is known about the potential for antibiotic migration from freestall dairy operations into groundwater (runoff to streams is prohibited). Dairies administer significantly less antibiotics per unit animal weight than other CAFO industries in accordance with the grade "A" Pasteurized Milk Ordinance, which prohibits administration of most antibiotics to lactating cows (*14*) except monensin, an ionophore used as a feed additive to increase milk production (*15*). However, antibiotics are prophylactically used on calves, heifers, and dry cows, raising concerns of significant antibiotic loading to the environment, especially in regions with high concentration of dairy farms.

This is the first study to comprehensively evaluate the fate of antibiotics in dairy operations, from administration to excretion, waste collection, land application, and potential soil–water transport under relatively vulnerable groundwater conditions. At two farm study sites, the major dairy management units were sampled, where each is characterized by specific antibiotic uses or waste management operations. Analysis of soil and water samples permitted us to assess the potential for off-site migration of antibiotics, and to identify environmental conditions that promote retention or on-site degradation of antibiotics.

Materials and Methods

The research dairies are located on the distal alluvial fans of the Stanislaus River and the Tuolomne River just east of the northern San Joaquin Valley trough. Groundwater levels at the study sites range from 2–5 m below ground surface. The dominant soil texture is sandy loam. The shallow saturated and overlying unsaturated zone consists of predominantly

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silty fine sand with intercalated, discontinuous clayey silt. The average regional groundwater flow rate is 5×10^{-7} m s^{-1} (*16*). Monitoring wells, located throughout the dairies (Supporting Information (SI) Figure S1), are screened from 3 to 10 m below ground surface. Shallow groundwater samples have a composite age ranging from weeks to approximately two years. The associated upgradient source area is 150 m to several hundred meters in length and a few to tens of meters in width (*16, 17*).

During the study, dairy I housed 1450 lactating cows, 1400 heifers, and 250 dry cows. Dairy II consisted of 1340 lactating cows, 1240 heifers, and 470 dry cows. Before weaning, calves are kept in individual hutches. Calf hutches are located on a raised structure at Dairy I. Its floor is flushed with clean groundwater three times per day. Calf hutches at Dairy II sit on bare ground. Heifers are kept in separate freestalls grouped by age. Adult cows are kept in freestalls and have access to adjacent exercise yards (corrals) between feedings. Freestall flush-lanes are lined with concrete, and are flushed three to four times per day with recycled lagoon water to collect excrement. Solid waste is separated from the waste stream, and recycled as bedding material in freestalls and exercise yards after drying. Wastewater is returned to the lagoon. Off-site runoff is not permitted. Corral surface runoff and dairy wash-water are collected in the lagoon. At both dairies, the lagoons were constructed over 30 years ago with a soil linear containing 10% clay. Liquid manure and unused solids are applied as fertilizer to surrounding forage fields, which typically comprise over 75% of the total farm area (*15*). Similar modern freestall dairy operations can be found worldwide.

For this study, the following dairy management units were sampled: calf hutches, hospital pens, liquid manure storage lagoons, solid and liquid manure applied fields, and corrals and freestalls for heifers, for milking cows, and for dry cows (*15*), (SI Figure S1). Environmental pathways that may allow antibiotics to be transported into groundwater include leakage from lagoons, leaching of manure applied to fields, and leaching from animal housing areas.

Samples were collected from surfaces (loose soil/litter materials), soil (<30 cm depth), wastewater, and shallow groundwater in four campaigns over 18 months representing fall, winter, spring, and summer climate conditions and operations status. Surface samples in the dairy production area were taken from bedding materials composed of dried solid manure, and those in the field were taken from loose surface soil. Concentrations of antibiotics were determined using online solid phase extraction (OLSPE) and liquid chromatography-tandem mass spectrometry (LC/MS/MS) with electrospray ionization (ESI) for water samples (*18*). Solid samples were extracted using the accelerated solvent extraction (ASE) method described in McKinney et al. (*19*) and analyzed by direct aqueous injection of the solid sample extracts using a Shimadzu Prominence LC and API 5000 tandem MS (Columbia, MD) in multiple-reaction-monitoring (MRM) mode with ESI and positive-negative ion switching (see SI for details).

Results and Discussion

Pharmaceutical Usage. A wide variety of pharmaceuticals were used in the study dairies, with total farm application rates varying from 0.02 to 660 g d^{-1} according to interviews with the participating farmers (Table 1). Substantial differences were observed between the types and quantities of pharmaceuticals applied at the two dairies. At both dairies, penicillin procaine G, monensin, and acetylsalicylic acid (aspirin) had the highest use (several hundred g d^{-1}), followed by ampicillin, ceftiofur, sulfonamides, and tetracyclines (several tens of g d^{-1}). Assuming no loss of antibiotics in the waste collection system by degradation or sorption, estimated worst-case antibiotic concentrations in lagoon water range from tens of ng L^{-1} to hundreds of μg L^{-1} (Table 1, details of the estimate are in SI Table S3).

Occurrence and Transport: Waste Management Systems. *Lagoon and Flush-Lane Water.* Sulfonamides and trimethoprim, tetracyclines and their epimers/isomers, and lincomycin were detected frequently in lagoon and flush-lane water samples with concentrations ranging from 0.012 to 267 μg L^{-1} (Table 2). Epimers/isomers of chlortetracycline were detected although the parent chlortetracycline was not present, whereas both tetracycline and its epimer were found when the concentration of tetracycline was close to 0.1 μg L^{-1}. Importantly, all antibiotics on the analytical schedule known to be administered at the farms were detected in lagoon and flush-lane water. The presence of the complete suite of administered antibiotics in the dairy waste system is consistent with the broad spectrum of human-applied pharmaceuticals found in municipal wastewater systems (*20*). It is possible that other pharmaceuticals used at these dairies but not on the analytical schedule were also present.

For the few studies which report antibiotics in dairy lagoon water, detections included tetracycline, iso-chlortetracycline, epi-iso-chlortetracycline, and lincomycin ranging from 0.01 to 7.7 μg L^{-1} (*3, 21*), similar to this study. The spectrum of antibiotics reported in swine lagoons is similar to those found in our study, with chlortetracycline, iso-chlortetracycline, epi-iso-chlortetracycline, lincomycin, oxytetracycline, sulfamethazine, tetracycline, sulfathiazole, tylosin, erythromycin-H_2O, and penicillin G frequently reported at concentrations ranging from high ng L^{-1} to low mg L^{-1} (*1, 3, 22, 23*). However, the lagoon water concentrations of antibiotics detected in this study were in the ng L^{-1} to low μg L^{-1} range, lower than those reported in swine lagoons. Lower antibiotics amounts administered, higher water use, and larger lagoon size, among other factors, may explain this difference. In particular, swine often receive antibiotics as feed additives (*24*), whereas antibiotic use in feed additives of dairy farms is limited. The spectrum of compounds detected in this study is similar to that in swine lagoons, suggesting similar transport processes and persistence in the waste-stream.

Observed concentrations of tetracycline, epi-tetracycline, chlortetracycline, iso-chlortetracycline, epi-so-chlortetracycline, lincomycin, and trimethoprim were at least 1 order of magnitude smaller than the theoretical maximum concentration estimated for lagoon water (Table 1, 2). In at least one sampling event, sulfonamide concentrations in the Dairy I lagoon were on the same order of magnitude as the theoretical maximum, suggesting that the attenuation of sulfonamides in the wastewater system may not always be significant.

The observed concentration variability was high (Table 2), possibly due to intermittent use of antibiotics. Freestall flush-lane water, recycled from the lagoons, was sampled to capture added antibiotics from feces and urine collected during flushing. However, the range of concentrations detected in flush-lane water was comparable to those in lagoon water samples. Hence, the concentration increase in flush water due to addition of antibiotics from fresh feces and urine was much smaller than lagoon water concentrations. Also, detected compounds apparently do not substantially degrade within the waste storage and recycling system.

The calf hutches flush used fresh groundwater rather than recycled lagoon water. It provided a better measure of antibiotics excretion. Relatively high concentrations of sulfamethazine, sulfamethoxazole, oxytetracycline, and trimethoprim, were detected there, reflecting the intensive use of antibiotics on calves and the significant contribution of fresh urine and feces to antibiotics in wastewater.

Lagoon Sediments. Sediments from a lagoon were collected to assess sediment-solution partitioning during percolation. Sulfamethazine (36 μg kg^{-1}), total chlortetracycline

TABLE 1. Pharmaceuticals Used in the Study Dairy Farms and Theoretical Maximum Concentrations in Lagoon Water[a]

class		use g d^{-1}		theoretical maximum concentration in lagoon[b] μg L^{-1}	
antibiotics	compound	Dairy I	Dairy II	Dairy I	Dairy II
aminoglycoside	dihydrostreptomycin	17.1		13	
beta-lactam	amoxicillin	0.05		0.1	
	ampicillin		31.3		76
	cloxacillin	0.13		0.1	
	penicillin procaine G	660.0	56.0	750	135
cephalosporin	ceftiofur	14.6	10.8	16	25
	cephapirin	0.1		0.1	
chloramphenicol derivative	florfenicol	2.5	1.9	2	3
lincosamide	**lincomycin**	6.0	5.5	8	15
	pirlimycin		0.03		0.1
macrolide	**tylosin**				
	erythromycin				
sulfonamides	**sulfadimethoxine**	24.3		5	
	sulfamethazine	8.8	10.8	1	3
	sulfamethoxazole	8.8		3	
tetracycline	**oxytetracycline**	7.1	2.6	8	6
	tetracycline				
	chlortetracycline				
other	**trimethoprim**	1.8		1	
ionophore	lasalocid	4.1		3	
	monensin	388.8	31.0	246	42
quinolone	decoquinate		7.2		17
anti-inflammatory					
non steroidal	acetylsalicylic acid	445.7	369.1	68	119
	flunixin meglumine		2.1		2
steroidal	isoflupredone acetate	0.02		0.03	
	dexamethasone	0.10	0.24	0.1	0.5
diuretic	furosemide	1.8	0.09	1	0.1

[a] Compounds in bold were analyzed in this study. The pharmaceuticals were identified and total masses used were obtained through interviews with the dairy owners and veterinary staff, and by examining the dairy's purchase receipts over the preceding 6- to 9-month period. The theoretical maximum is the total mass of pharmaceutical excreted divided by the lagoon volume. The details of the estimate are in the SI. Theoretical maximum concentration in lagoon = use × excretion rate × retention time/lagoon volume. Lagoon volumes are 6.66×10^4 m^3 (Dairy I) and 8.98×10^4 m^3 (Dairy II). Retention times (84.1 d (Dairy I) and 241 d (Dairy II)) are calculated using the daily water use estimate proposed by Meyer et al. (*55*). See SI for details on excretion rate. [b] Theoretical maximum concentrations were estimated assuming no attenuation.

(176 μg kg^{-1}), oxytetracycline (109 μg kg^{-1}), and tetracycline (42 μg kg^{-1}) were detected in a lagoon sediment sample (Table 2). The apparent distribution coefficients ($K_{d\ app}$) between the lagoon water and the sediment for sulfamethazine and oxytetracycline were 8.3 and 351 L kg^{-1}, respectively. The $K_{d\ app}$ value of oxytetracycline was somewhat greater than the reported K_d values of 77.6 L kg^{-1} in swine manure (*25*). Compared to the K_d values in soils or soil constituents, $K_{d\ app}$ of sulfamethazine is greater than the reported range (0.6−3.1 L kg^{-1}), and $K_{d\ app}$ of oxytetracycline is within the reported range (0.3−3020 L kg^{-1}) (*26, 27*). The $K_{d\ app}$ value is subject to variations in sorbent and aqueous phase properties. In the lagoon water/sediment system, where pH is often near or above pK_{a2} of tetracyclines and sulfonamides, zwitterionic or anionic species are dominant for tetracyclines, and neutral and anionic species are dominant for sulfonamides, which will result in a decrease of the K_d values.

We are not aware of previous studies on antibiotics in CAFO lagoon sediments. Our data suggest that these sediments play a significant role as a sink/source of antibiotics leached by percolating lagoon water (*17*). Further, some farms apply lagoon sediments to their fields as soil amendments (*28*).

Lagoon-Impacted Groundwater. Shallow groundwater samples were collected 10 m downgradient of the dairy lagoons ("lagoon wells") to assess antibiotics in anoxic lagoon leakage plumes in shallow groundwater (*16*). Of the 10 compounds that were detected in lagoon water, only sulfadimethoxine, sulfamethazine, and lincomycin were detected in groundwater. Seven compounds present in lagoon water were attenuated to levels below the detection limit - sulfamethoxazole and trimethoprim likely due to biodegradation (*29, 30*), tetracyclines likely due to sorption and abiotic degradation (*31, 32*). Lagoon well samples at Dairy I showed higher concentrations ranging from 0.033 to 0.13 μg L^{-1} for sulfadimethoxine, and 1.1 to 3.6 μg L^{-1} for sulfamethazine, consistent with higher concentrations of sulfadimethoxine and sulfamethazine in lagoon water at Dairy I.

Elsewhere, concentrations of sulfadimethoxine (0.076−0.22 μg L^{-1}), sulfamethazine (0.046−0.067, up to 0.16 μg L^{-1}),

TABLE 2. Antibiotics Concentrations in Wastewater Collection/Treatment System and Associated Shallow Groundwater[a]

dairy	sample	date sampled	sulfadimethoxine	sulfamethazine	sulfamethoxazole	*iso-chlortetracycline	*epi-iso-chlortetracycline	total chlortetracycline	oxytetracycline	tetracycline	*epi-tetracycline	lincomycin	trimethoprim
							μg L^{-1}						
1. water samples													
(1) wastewater													
Dairy I	lagoon water	October, 06	0.040	6.0	0.88	–	–	NA	0.093	–	–	–	–
		April, 07	11	14	–	1.5	1.0	NA	–	0.020	–	–	–
		September,07	9.0	4.4	4.9	–	–	NA	0.31	–	–	–	0.024
		January, 08	4.1	8.6	0.43	0.99	0.68	NA	0.66	0.11	0.38	–	–
	flush-lane water	October, 06	–	5.5	2.0	–	–	NA	–	–	–	–	–
		April, 07	3.4	5.7	–	1.2	0.77	NA	–	0.14	0.022	–	–
		September, 07	0.62	0.26	0.69	–	–	NA	–	–	–	–	–
		January, 08	7.5	8.9	0.19	0.28	0.19	NA	0.090	0.028	–	–	–
	calf hutches flush water	October, 06	–	15	19	–	–	NA	–	–	–	–	–
		May, 07	–	–	2.0	–	–	NA	0.076	–	–	–	0.23
		September, 07	–	0.63	1.5	0.017	–	NA	0.80	–	–	–	0.035
		January, 08	NC	NC	NC	NC	NC	NA	NC	NC	NC	NC	NC
Dairy II	lagoon water	October, 06	0.25	–	–	–	–	NA	0.19	0.087	–	0.054	–
		April, 07	0.56	–	–	–	–	NA	0.10	0.074	–	0.044	–
		September, 07	0.030	–	–	–	–	NA	–	–	–	0.012	–
		January, 08	0.77	0.61	–	0.12	0.083	NA	0.18	0.095	0.035	–	–
	flush-lane water	October, 06	0.19	–	–	–	–	NA	0.12	0.060	–	0.035	–
		April, 07	0.25	–	–	–	–	NA	0.19	0.14	0.089	0.061	–
		September, 07	0.035	–	–	–	–	NA	–	–	–	–	–
		January, 08	–	–	1.7	252	267	NA	0.52	3.1	2.8	–	2.3
(2) lagoon well groundwater													
Dairy I	well no. 3	October, 06	NC	NC	–	–	–	NA	–	–	–	NC	–
		April, 07	0.098	2.8	–	–	–	NA	–	–	–	0.23	–
		September, 07	0.13	3.6	–	–	–	NA	–	–	–	–	–
		January, 08	0.033	1.1	–	–	–	NA	–	–	–	0.082	–
Dairy II	well no. 3	October, 06	0.017	0.29	–	–	–	NA	–	–	–	–	–
		April, 07	–	–	–	–	–	NA	–	–	–	1.9	–
		September, 07	–	–	–	–	–	NA	–	–	–	1.1	–
		January, 08	NC	NC	–	–	–	NA	–	–	–	NC	–
(3) manure-treated field groundwater													
Dairy I	well no. 7	October, 06	0.005	0.037	–	–	–	NA	–	–	–	–	–
		April, 07	–	–	–	–	–	NA	–	–	–	–	–
		September, 07	0.010	0.052	–	–	–	NA	–	–	–	–	–
		January, 08	–	0.029	–	–	–	NA	–	–	–	–	–
	well no. 9	October, 06	0.006	0.044	–	–	–	NA	–	–	–	–	–
		April, 07	–	0.060	–	–	–	NA	–	–	–	–	–
		September, 07	–	0.061	–	–	–	NA	–	–	–	–	–
		January, 08	–	0.11	–	–	–	NA	–	–	–	–	–
	well no. 11	October, 06	–	–	–	–	–	NA	–	–	–	–	–
		April, 07	–	–	–	–	–	NA	–	–	–	–	–
		September, 07	–	–	–	–	–	NA	–	–	–	–	–
		January, 08	–	0.007	–	–	–	NA	–	–	–	–	–

TABLE 2. Continued

dairy	sample	date sampled	sulfadimethoxine	sulfamethazine	sulfamethoxazole	*iso-chlortetracycline	*epi-iso-chlortetracycline	total chlortetracycline	oxytetracycline	tetracycline	*epi-tetracycline	lincomycin	trimethoprim
			μg kg^{-1}										
	2. solid samples												
Dairy I	lagoon sediment	August, 07	–	36	–	NA	NA	176	109	42	–	–	–
	manure-treated field												
Dairy II	surface sample	October, 06	–	–	6.2	NA	NA	–	25	105	163	–	–
		April, 07	–	–	–	NA	NA	–	–	–	–	–	–
		September, 07	–	–	–	NA	NA	–	–	8.8	–	–	–

[a] Units and wells not identified had no detectable concentrations over the course of the study. *: degradation product, –: below detection, NA: not analyzed, NC: not collected. Below detection: Dairy I: groundwater: well no. 12, surface samples: manured field, soil samples: manured field. Dairy II: soil: manured field. Below detection in water samples: Carbamazapine, Azithromycin, Erythromycin, *Erythromycin-H_2O, Roxithromycin, Tylosin, Virginiamycin, Ciprofloxacin, Lomefloxacin, Norfloxacin, Ofloxacin, Sarafloxacin, Enrofloxacin, Sulfachloropyridazine, Sulfadiazine, Sulfathiazole, Chlorotetracycline, *Epi-chlorotetracycline, Doxycyline, *Epi-oxytetracycline, Chloramphenicol, Ormetoprim. Below detection in solid samples: Carbamazapine, total Erythromycin A, Roxithromycin, Tylosin, Virginiamycin, Ciprofloxacin, Lomefloxacin, Norfloxacin, Ofloxacin, Sarafloxacin, Enrofloxacin, Sulfachloropyridazine, Sulfadiazine, Sulfathiazole, Doxycyline, Chloramphenicol, Ormetoprim, Trimethoprim.

sulfamethoxazole (up to 0.47 μg L^{-1}), and lincomycin (1.4 μg L^{-1}) have been reported at similar concentrations in groundwater impacted by agriculture (*33*), beef feedlots (*34*), and swine lagoons (*1*). In our study, sulfamethazine concentrations were higher than previously reported, while sulfamethoxazole was below the detection limit.

Interestingly, lincomycin was found in groundwater at Dairy I even though it was not found in lagoon water. Also, it was found in groundwater at Dairy II at higher concentrations than in lagoon water. This may reflect historic use of lincomycin as shallow groundwater is up to two years old (*16, 17*). In addition, the mode of administration of lincomycin is unique in that it is topically applied as powder in bandage on infected hooves during dry periods, whereas other antibiotics are administered systemically through injection, orally, or intramammary. The bandages should be removed after 2–5 days, but in practice they may be left to fall off, leaving the lincomycin powders remaining in the discarded bandage on the ground (*35*). With dry cows housed near the lagoon wells at both of the dairies, it is possible that lincomycin leached from the corral area. The persistence of lincomycin in this study is consistent with its known chemical (*32, 36*), photochemical (*36*) and microbial (*37*) stability.

Surface and Soil Samples in Manure-Applied Fields. Forage-field applications of lagoon water and manure solids represent a potential pathway for off-site migration of antibiotics into groundwater driven by recharge from irrigation or precipitation. Surface samples from fields on Dairy II contained sulfamethoxazole (6.2 μg kg^{-1}), oxytetracycline (25 μg kg^{-1}), tetracycline (8.8–105 μg kg^{-1}), and epi-tetracycline (163 μg kg^{-1}), providing evidence of environmental persistence. However, no antibiotics were detected in the manure-treated field surface samples at Dairy I, or in underlying soil samples (<30 cm depth) at either dairy, suggesting surface processes can be effective at attenuating these compounds to levels below detection. There were no detections in surface and soil samples from control fields without manure applications.

Groundwater Underneath Manure-Treated Fields. Sulfadimethoxine and sulfamethazine were detected in monitoring wells next to a field that received lagoon water at Dairy I, despite the fact that no antibiotics were detected in surface or soil samples. At Dairy I, sulfamethazine was detected consistently at field wells nos. 7 and 9 at concentrations ranging from 0.029 to 0.11 μg L^{-1}, and sporadically at well no. 11. These wells are located proximal to outlet valves of the lagoon-water flood irrigation system, where infiltration rates into soils maybe higher than elsewhere in the field. Detection of sulfadimethoxine was less frequent and close to the detection limit (0.005 μg L^{-1}) at nos. 7 and 9. Persistence of sulfamethazine may be attributed to the lack of anaerobic degradability (*30*). There were no detections at wells located distant from the flood irrigation outlet (no. 12 at Dairy I). Thus it appears that sulfonamides in applied lagoon water are readily transported into shallow groundwater, but do not persist in soil or at the land surface. Tetracyclines, on the other hand, are more strongly sorbed and persist at the soil surface where they are degraded. No antibiotics were detected in shallow groundwater from control wells not affected by dairy activities (Dairy I: well no. 10, Dairy II: well no. 6).

Our findings are consistent with previous studies that have observed tetracyclines in shallow soil layers and sulfonamides in leachate and groundwater. Sulfonamides weakly sorb to soils, with K_d values in the range of 10° to 10^1 L kg^{-1} (*26, 27, 38, 39*), whereas tetracyclines show higher sorption, with K_d values from 10^2 to 10^6 L kg^{-1} (*26, 27, 40*). One of the reasons for this difference is that tetracyclines intercalate between swelling clay layers while sulfonamides do not (*41, 42*). As a result sulfonamides persist in groundwater (*43, 44*), while tetracyclines persist in soil (*2, 43, 45–47*).

TABLE 3. Antibiotics Concentrations in Dairy Production Areas and Associated Shallow Groundwater[a]

dairy	sample	date sampled	tylosin	sulfadimethoxine	sulfamethazine	sulfamethoxazole	oxytetracycline	tetracycline	*epi-tetracyucline	total chlortetracyclines	total erythromycin A	lincomycin
	1. goundwater samples, dairy production area						μg L^{-1}					
Dairy I	well no. 4	October, 06	–	–	–	–	–	–	–	NA	NA	–
		April, 07	–	–	–	–	–	–	–	NA	NA	–
		September, 07	–	0.005	–	–	–	–	–	NA	NA	–
		January, 08	–	–	–	–	–	–	–	NA	NA	–
Dairy II	well no. 1	October, 06	0.025	–	0.14	–	–	–	–	NA	NA	–
		April, 07	NC	NC	NC	NC	NC	NC	NC	NA	NA	NC
		September, 07	–	–	0.088	–	–	–	–	NA	NA	–
		January, 08	–	–	0.069	–	–	–	–	NA	NA	–
	2. solid samples (1) surface samples						μg kg^{-1}					
Dairy I	lactating cow freestall	October, 06	–	–	–	–	–	–	–	–	–	–
		April, 07	–	–	–	–	–	–	–	–	–	–
		September, 07	–	–	–	–	40	5.6	–	9.7	–	–
	lactating cow	October, 06	–	–	–	–	–	–	–	–	>1000	–
	exercise yard	April, 07	–	–	–	–	–	–	–	–	–	–
		September, 07	–	–	7.5	–	–	–	–	–	–	–
	hospital pen	October, 06	–	6.9	–	–	–	73	–	–	–	–
		April, 07	–	248	–	–	–	50	–	–	–	–
		September, 07	–	457	–	–	11	46	–	–	–	–
	heifer exercise yard	October, 06	–	–	–	–	–	–	–	–	–	–
		May,07	–	–	–	–	–	–	–	–	–	–
		September, 07	–	6.4	–	–	24	–	–	–	–	–
Dairy II	lactating cow	October, 06	–	–	–	–	7.9	–	–	–	–	–
	freestall	April, 07	–	–	–	–	–	–	–	–	–	–
		September, 07	–	–	–	–	–	–	–	–	–	–
	lactating cow	October, 06	–	–	10	36	–	–	–	–	–	–
	exercise yard	April, 07	–	–	–	–	–	–	–	–	–	–
		September, 07	–	–	–	–	–	–	–	–	–	–
	hospital pen	October, 06	–	5.8	–	–	18	19	–	–	–	–
		April, 07	–	–	–	–	–	6.2	11	–	–	–
		September, 07	–	43	–	–	–	–	–	–	–	–
	heifer exercise yard	October, 06	–	–	–	–	–	–	–	–	–	–
		May,07	–	–	–	–	–	–	–	–	–	–
		September, 07	–	–	–	–	188	–	–	–	–	–
	calf hutches	October, 06	–	–	–	–	–	–	–	–	–	–
		May,07	–	–	–	–	556	–	–	–	–	–
		September, 07	–	–	–	–	–	–	–	–	–	–

TABLE 3. Continued

dairy	sample	date sampled	tylosin	sulfadimethoxine	sulfamethazine	sulfamethoxazole	oxytetracycline	tetracycline	*epi-tetracyucline	total chlortetracyclines	total erythromycin A	lincomycin
(2) Soil												
Dairy II	lactating cow freestall	August, 07	–	–	–	–	–	19	–	–	–	–
	lactating cow exercise yard	August, 07	–	–	–	11	–	–	–	–	–	–
	hospital pen	August, 07	–	15	–	–	–	30	–	–	–	–

[a] Units and wells not identified had no detectable concentrations over the course of the study. *: degradation product, –: below detection, NA: not analyzed, NC: not collected. Below detection: Dairy I: Groundwater: well no. 1, soil: lactating cow freestall, lactating cow exercise yard. Dairy II: Groundwater: well nos. 2, 4, 5, 7, 8, soil: heifer yard, calf hutches. Below detection in water samples: Carbamazapine, Azithromycin, Erythromycin, *Erythromycin-H_2O, Roxithromycin, Virginiamycin, Ciprofloxacin, Lomefloxacin, Norfloxacin, Ofloxacin, Sarafloxacin, Enrofloxacin, Sulfachloropyridazine, Sulfadiazine, Sulfathiazole, Chlorotetracycline, *Epi-chlorotetracycline, *Epi-iso-chlorotetracycline, *Iso-chlorotetracycline, Doxycyline, *Epi-oxytetracycline, Chloramphenicol, Ormetoprim, Trimethoprim. Below detection in solid samples: Carbamazapine, Roxithromycin, Virginiamycin, Ciprofloxacin, Lomefloxacin, Norfloxacin, Ofloxacin, Sarafloxacin, Enrofloxacin, Sulfachloropyridazine, Sulfadiazine, Sulfathiazole, Doxycyline, Chloramphenicol, Ormetoprim.

Occurrence and Transport: Animal Production Area. *Surface and Soil Samples.* The main sources of antibiotics in the animal production area are feces and urine excrements, accumulating in a spatially heterogeneous pattern. Consequently, concentration variability was high despite compositing samples from 12 separate locations across each management unit (Table 3). Sulfonamides (mainly sulfadimethoxine) and tetracyclines were frequently detected in surface samples. High variability was most evident for erythromycin in the lactating cow exercise yard at Dairy I, and for oxytetracycline in the heifer exercise yard and in the calf hutch area at Dairy II: Each was detected at high concentrations (188 to >1000 μg kg^{-1}) once, but was below detection limit at other sampling times. This suggests a very high concentration in one or a few of the samples composited for analysis, which likely resulted from intermittent and spatially variable patterns of administration and excretion. At the two dairies, antibiotics (except monensin at Dairy I) are not administered as feed additives. Only a small number of animals are under treatment at any given time, which results in spatially and temporally variable detections.

Antibiotics were frequently detected in surface samples of hospital pens at both of the dairies. Sulfadimethoxine (5.8−457 μg kg^{-1}) and tetracycline (6.2−73 μg kg^{-1}) were most common. Detections of other antibiotics at hospital pens included oxytetracycline (11 and 18 μg kg^{-1}), and epi-tetracycline (11 μg kg^{-1}).

Detections were sporadic in the surface samples of lactating cow freestalls, lactating cow exercise yard, heifer exercise yard, and calf hutches. Concentrations were similar to those reported elsewhere (*48–50*). We anticipated that high usage of antibiotics in calf hutches would yield numerous detections samples from Dairy II, but obtained few. Limited detections in surface samples at calf hutches at Dairy II were surprising also in light of the frequent and high detections in wastewater samples from calf hutches at Dairy I. We speculate that sulfonamides, which are commonly administered to calves, show low sorption to soils (*26, 27*).

Soil samples (0−30 cm depth) were used to assess infiltration via pore water and to evaluate storage and buffering by soils during infiltration. Soil samples yielded a different pattern of occurrence from that seen in surface samples. At Dairy I, all antibiotics were below detection in samples from lactating cow freestall soils and from lactating cow exercise yard soils, even though sulfamethazine, oxytetracycline, tetracycline, chlortetracycline, and erythromycin A were sporadically detected in surface samples. At Dairy II, sulfamethoxazole was detected in both surface and soil samples from the lactating cow exercise yard; sulfadimethoxine and tetracycline were detected in surface and soil samples from the hospital pen, all at similar concentration levels (11 to 30 μg kg^{-1}, Table 3). Tetracycline was detected in soil of the lactating cow freestalls at Dairy II, but not in their surface samples. This is likely due to intermittent administration and spatial variability. There were no detections in heifer exercise yard soil and calf hutch soils at Dairy II. Overall, the detection of several antibiotics in soil samples indicates differential mobility of antibiotics in the subsurface environment. Hence, the production area of dairies—even outside the lagoon—cannot be ruled out as a potential source of antibiotics in groundwater.

Production Area Groundwater. Shallow groundwater was sampled from wells associated with animal production areas to assess the migration of antibiotics into groundwater. Sulfamethazine was found in well no. 1 (Dairy II) for all sampling campaigns, ranging from 0.088 to 0.14 μg kg^{-1}. Well no. 1 is near freestalls, near the feed and manure solids storage areas, and near possibly leaking, buried flush water pipelines. Tylosin and sulfadimethoxine were also detected in ground-

TABLE 4. Approximate Mass of Antibiotics [g] within Lagoons, Groundwater, Management Unit Surface, and Within the 0−30 cm Soil Horizon Calculated by Multiplying the Average Concentration with the Lagoon Volume, Groundwater Volume in the Monitoring Well Source Area and Areas of Each Management Unit, Respectively[a]

	Dairy I					Dairy II			
	lagoon	lagoon sediments	ground water	surface	soil	lagoon	ground water	surface	soil
tylosin	−	−	−	−	−	−	0.01	−	−
sulfadimethoxine	402	−	0.1	34	−	36	0.01	1	7
sulfamethazine	550	316	4.1	6	−	14	0.3	9	170
sulfamethoxazole	103	−	−	4	−	−	−	31	−
total chlorotetracycline	−	1543	−	1	−	−	−	−	−
iso-chlorotetracycline	42	−	−	−	−	3	−	−	−
epi-iso-chlortetracycline	29	−	−	−	−	2	−	−	−
oxytetracycline	18	956	−	30	−	11	−	180	−
tetracycline	2	368	−	76	−	6	−	1	55
epi-tetracycline	6	−	−	98	−	1	−	0.3	−
lincomycin	−	−	0.2	−	−	3	2.2	−	−
trimethoprim	0.4	−	−	−	−	−	−	−	−
total erythromycin A	−	−	−	767	−	−	−	−	−

[a] Assumptions are well source area 15 m wide by 100 m long and affecting an average depth below the water table of 3.5 m with aquifer porosity of 30%, surface depth 5 cm, soil depth 30 cm, the soil density 1.8 g cm^{-3}, the lagoon sediment depth 0.8m, the lagoon sediment density 1.0 g cm^{-3}, and lagoon sediment moisture content 40%. Lagoon sediments at Dairy II were not collected.

water below animal production areas, but the detections were sporadic.

Comparing Shallow Groundwater Impact. Our study indicates that antibiotics occur ubiquitously at the surface and in the waste-stream of dairy farms, but do not extensively accumulate in soils. They are not generally transported in groundwater beyond the boundaries of the farm—even after decades of use. Sulfonamides, tetracyclines, and their epimers/isomers, and lincomycin were most commonly detected. Tetracyclines and sulfonamides yielded contrasting patterns of occurrence in soils due to their different physicochemical properties. Lincomycin persisted in groundwater, but was not detected in surface or soil samples. Sorption of lincomycin to clay by cation exchange can potentially be significant, but may be inhibited due to high pH, lack of clay minerals with high cation exchange capacity and/or surface area, or the presence of competing cations (*51*).

Based on measured average antibiotic concentrations, total quantities of antibiotics present at the study farms can be computed (Table 4). The known antibiotics mass in groundwater is small compared to other environmental compartments, partly due to the limited extend of the source area associated with the monitoring wells. Tetracyclines exist mainly in lagoon sediments and surface samples while sulfonamides are dominant in lagoon water. The mass of sulfamethazine is also significant in lagoon sediments.

Importantly, sulfamethazine concentrations in the animal production area groundwater were an order of magnitude lower, and those in groundwater from manure-treated fields were 2 orders of magnitude lower than in the lagoon seepage plume (lagoon wells). Furthermore, the concentration in field wells decreased with distance from the flood irrigation system outlet to below detection, similar in occurrence to monensin (*15*). A considerable loss of sulfonamides in soil pore water and in leachate was observed elsewhere with concentration distributions indicating preferential flow (*39, 52*).

These differences in shallow groundwater antibiotics concentrations are partly attributable to differences in loading rates: Lagoons continuously supply antibiotics-containing water to the lagoon plume, while the animal production area receives intermittent, spatially heterogeneous loading, albeit at possibly high concentrations. Manure and lagoon-water application to fields are infrequent and diluted with irrigation water. Based on known hydrologic fluxes and nutrient management practices (*17*), we estimate that the annual average net application of liquid manure in fields is 5 times lower than the potential leaching rate from lagoons. This is consistent with a nearly 2-fold difference in groundwater salinity, a conservative measure of the manure-derived fraction of groundwater (*16*).

After accounting for dilution, biochemical sulfonamide attenuation below fields is between 1 and 2 orders of magnitude larger than below the lagoon or below the production areas. Differences in oxygen content and redox conditions along the flowpaths, and in the concentrations of sulfonamides (*53*) may explain the contrast in biodegradation between these sites: An anaerobic zone exists below the lagoon and extends for at least a few tens of meters (laterally) into the shallow groundwater (*16, 54*), whereas irrigation water mixed with lagoon water during flood irrigation is sufficiently high in dissolved oxygen to permit aerobic degradation in the subsurface of the field well source area. Production area groundwater also has low redox potential with very low oxygen content. This is consistent with previous work indicating that the major attenuation process of sulfonamides is aerobic biodegradation, but not complete mineralization to CO_2, and sorption of the degradation products to soil (*52*). In addition, Wang et al. showed that sulfadimethoxine biodegradation is faster when the initial concentrations are lower (low mg kg^{-1} range) (*53*). However, it is not clear if this qualitative relationship between biodegradation and initial concentration can be extrapolated to liquid concentrations at the ng L^{-1} level observed here.

Our results suggest that sulfonamide attenuation can be improved by proper dilution of lagoon water with irrigation water and control of the loading rate. This will provide sufficient labile organic matter to stimulate microbial activity, while avoiding pervasive anaerobic conditions. Longer flowpaths to promote sorption may further facilitate concentration reduction in groundwater. Future research is needed to identify attenuation mechanisms that can be tied to specific best management practices (BMP) including dilution ratio and irrigation practices to optimally promote degradation and sorption.

Further research must assess whether the low but continuous occurrence of antibiotics at the farm surface affects the ecosystem and microbial community including development of antibiotic resistance. Localized high concentrations of antibiotics at dairy facility surfaces also suggest that the atmospheric pathway via dust emissions deserves close attention. Degradation pathways and physicochemical and degradation properties of parent and degradation compounds urgently need further study and aggregation into a publicly accessible database.

Importantly, our work shows that the distinction of management units by antibiotic use patterns and by operational system is important to understanding the occurrence of these compounds in animal farming operations. The large spatial and temporal variability suggests that intensive sampling campaigns are necessary to properly evaluate animal farms as sources of antibiotics.

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Supporting Information Available

Analytical methods, study-site farm layouts, theoretical worst-case maximum lagoon concentration estimate.This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) Campagnolo, E. R.; Johnson, K. R.; Karpati, A.; Rubin, C. S.; Kolpin, D. W.; Meyer, M. T.; Esteban, J. E.; Currier, R. W.; Smith, K.; Thu, K. M.; McGeehin, M. Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. *Sci. Total Environ.* **2002**, *299* (1−3), 89–95.

(2) Hamscher, G.; Sczesny, S.; Hoper, H.; Nau, H. Determination of persistent tetracycline residues in soil fertilized with liquid manure by high-performance liquid chromatography with electrospray ionization tandem mass spectrometry. *Anal. Chem.* **2002**, *74* (7), 1509–1518.

(3) Bradford, S. A.; Segal, E.; Zheng, W.; Wang, Q.; Hutchins, S. R. Reuse of Concentrated Animal Feeding Operation Wastewater on Agricultural Lands. *J. Environ. Qual.* **2008**, S97–S115.

(4) Cromwell, G. L.; Davis, G. W.; Morrow, W. E. M.; Primo, R. A.; Rozeboom, D. W.; Sims, M. D.; Stanisiewski, E. P.; Ho, C. H. Efficacy of the antimicrobial compound U-82,127 as a growth promoter for growing-finishing pigs. *J. Anim. Sci.* **1996**, *74* (6), 1284–1287.

(5) Animal Health Institute News release: Sales of Disease-Fighting Animal Medicines Rise. http://www.ahi.org/files/Media%20Center/Antibiotic%20Use%202007.pdf (accessed July 22, 2010).

(6) Boxall, A. B. A.; Kolpin, D. W.; Surensen, B. H.; Tolls, J. Are veterinary medicines causing environmental risks. *Environ. Sci. Technol.* **2003**, *37*, 265A–304A.

(7) Wollenberger, L.; Halling-Sorensen, B.; Kusk, K. O. Acute and chronic toxicity of veterinary antibiotics to Daphnia magna. *Chemosphere* **2000**, *40* (7), 723–730.

(8) Fernandez, C.; Alonso, C.; Babin, M. M.; Pro, J.; Carbonell, G.; Tarazona, J. V. Ecotoxicological assessment of doxycycline in aged pig manure using multispecies soil systems. *Sci. Total Environ.* **2004**, *323* (1−3), 63–69.

(9) Schmitt, H.; Van Beelen, P.; Tolls, J.; Van Leeuwen, C. L. Pollution-induced community tolerance of soil microbial communities caused by the antibiotic sulfachloropyridazine. *Environ. Sci. Technol.* **2004**, *38* (4), 1148–1153.

(10) Chee-Sanford, J. C.; Aminov, R. I.; Krapac, I. J.; Garrigues-Jeanjean, N.; Mackie, R. I. Occurrence and diversity of tetracycline resistance genes in lagoons and groundwater underlying two swine production facilities. *Appl. Environ. Microbiol.* **2001**, *67* (4), 1494–1502.

(11) Sengelov, G.; Agerso, Y.; Halling-Sorensen, B.; Baloda, S. B.; Andersen, J. S.; Jensen, L. B. Bacterial antibiotic resistance levels in Danish farmland as a result of treatment with pig manure slurry. *Environ. Int.* **2003**, *28* (7), 587–595.

(12) Sengelov, G.; Halling-Sorensen, B.; Aarestrup, F. M. Susceptibility of Escherichia coli and Enterococcus faecium isolated from pigs and broiler chickens to tetracycline degradation products and distribution of tetracycline resistance determinants in E-coli from food animals. *Vet. Microbiol.* **2003**, *95* (1−2), 91–101.

(13) *California Agricultural Directory 2008−2009*; California Department of Food and Agriculture: Sacramento, CA, 2009.

(14) *Grade "A" Pasteurized Milk Ordinance*, (2007 Revision); USPHS/FDA, Department of Health and Human Services, Public Health Service, Food and Drug Administration, Milk Safety Branch: College Park, MD, 2007.

(15) Watanabe, N.; Harter, T.; Bergamaschi, B. A. Environmental occurrence and shallow ground water detection of the antibiotic monensin from dairy farms. *J. Environ. Qual.* **2008**, *37* (5), S78–S85.

(16) Harter, T.; Davis, H.; Mathews, M. C.; Meyer, R. D. Shallow groundwater quality on dairy farms with irrigated forage crops. *J. Contam. Hydrol.* **2002**, *55* (3−4), 287–315.

(17) van der Schans, M. L.; Harter, T.; Leijnse, A.; Mathews, M. C.; Meyer, R. D. Characterizing sources of nitrate leaching from an irrigated dairy farm in Merced County, California. *J. Contam. Hydrol.* **2009**, (110), 9–21.

(18) Meyer, M. T.; Lee, E. A.; Ferrell, G. M.; Bumgarner, J. E.; Varns, J. Evaluation of offline tandem and online solid-phase extraction with liquid chromatography/electrospray ionization-mass spectrometry for analysis of antibiotics in ambient water and comparison to an independent method. In *U. S. Geological Survey Scientific Investigations Report 2007−5021*; U.S. Geological Survey: Reston, VA, 2007.

(19) McKinney, C.; Loftin, K.; Meyer, M.; Davis, J.; Pruden, A. Antibiotic resistance genes in livestock lagoons of various operation type, configuration, and antibiotic occurrence. *Environ. Sci. Technol.* **2010**, *44* 1947−1953.

(20) Targeted National Sewage Sludge Survey Sampling and Analysis Technical Report; U.S. Environmental Protection Agency: Washington, DC, 2009.

(21) Brown, K. D.; Kulis, J.; Thomson, B.; Chapman, T. H.; Mawhinney, D. B. Occurrence of antibiotics in hospital, residential, and dairy, effluent, municipal wastewater, and the Rio Grande in New Mexico. *Sci. Total Environ.* **2006**, *366* (2−3), 772–783.

(22) Meyer, M. T.; Bumgarner, J. E.; Varns, J. L.; Daughtridge, J. V.; Thurman, E. M.; Hostetler, K. A. Use of radioimmunoassay as a screen for antibiotics in confined animal feeding operations and confirmation by liquid chromatography/mass spectrometry. *Sci. Total Environ.* **2000**, *248* (2−3), 181–187.

(23) Aga, D. S.; Goldfish, R.; Kulshrestha, P. Application of ELISA in determining the fate of tetracyclines in land-applied livestock wastes. *Analyst* **2003**, *128* (6), 658–662.

(24) *Swine 2006, Part III: Reference of Swine Health, Productivity, and General Management in the United States, 2006*; USDA: APHIS:VS, CEAH: Fort Collins, CO, 2008.

(25) Loke, M. L.; Tjornelund, J.; Halling-Sorensen, B. Determination of the distribution coefficient (log K_d) of oxytetracycline, tylosin A, olaquindox and metronidazole in manure. *Chemosphere* **2002**, *48* (3), 351–361.

(26) Tolls, J. Sorption of veterinary pharmaceuticals in soils: A review. *Environ. Sci. Technol.* **2001**, *35* (17), 3397–3406.

(27) Thiele-Bruhn, S. Pharmaceutical antibiotic compounds in soils—A review. *J. Plant Nutr. Soil Sci.* **2003**, *166* (2), 145–167.

(28) Meyer, D. M.; Garnett, I.; Guthrie, J. C. A survey of dairy manure management practices in California. *J. Dairy Sci.* **1997**, *80* (8), 1841–1845.

(29) Ingerslev, F.; Halling-Sorensen, B. Biodegradability properties of sulfonamides in activated sludge. *Environ. Toxicol. Chem.* **2000**, *19* (10), 2467–2473.

(30) Mohring, S. A. I.; Strzysch, I.; Fernandes, M. R.; Kiffmeyer, T. K.; Tuerk, J.; Hamscher, G. Degradation and elimination of various sulfonamides during anaerobic fermentation: A promising step on the way to sustainable pharmacy. *Environ. Sci. Technol.* **2009**, *43* (7), 2569–2574.

(31) Kim, S.; Eichhorn, P.; Jensen, J. N.; Weber, A. S.; Aga, D. S. Removal of antibiotics in wastewater: Effect of hydraulic and solid retention times on the fate of tetracycline in the activated sludge process. *Environ. Sci. Technol.* **2005**, *39* (15), 5816–5823.

(32) Loftin, K. A.; Adams, C. D.; Meyer, M. T.; Surampalli, R. Effects of ionic strength, temperature, and pH on degradation of selected antibiotics. *J. Environ. Qual.* **2008**, *37* (2), 378–386.

(33) Hirsch, R.; Ternes, T.; Haberer, K.; Kratz, K. L. Occurrence of antibiotics in the aquatic environment. *Sci. Total Environ.* **1999**, *225* (1−2), 109–118.

(34) Batt, A. L.; Snow, D. D.; Aga, D. S. Occurrence of sulfonamide antimicrobials in private water wells in Washington County, Idaho, USA. *Chemosphere* **2006**, *64* (11), 1963–1971.

(35) Berry, S. L., Personal communication. In2009.
(36) Andreozzi, R.; Canterino, M.; Lo Giudice, R.; Marotta, R.; Pinto, G.; Pollio, A. Lincomycin solar photodegradation, algal toxicity and removal from wastewaters by means of ozonation. *Water Res.* **2006**, *40* (3), 630–638.
(37) Watkinson, A. J.; Murby, E. J.; Costanzo, S. D. Removal of antibiotics in conventional and advanced wastewater treatment: Implications for environmental discharge and wastewater recycling. *Water Res.* **2007**, *41*, 4164–4176.
(38) Boxall, A. B. A.; Blackwell, P.; Cavallo, R.; Kay, P.; Tolls, J. The sorption and transport of a sulphonamide antibiotic in soil systems. *Toxicol. Lett.* **2002**, *131* (1−2), 19–28.
(39) Burkhardt, M.; Stamm, C. Depth distribution of sulfonamide antibiotics in pore water of an undisturbed loamy grassland soil. *J. Environ. Qual.* **2007**, *36* (2), 588–596.
(40) Sassman, S. A.; Lee, L. S. Sorption of three tetracyclines by several soils: Assessing the role of pH and cation exchange. *Environ. Sci. Technol.* **2005**, *39* (19), 7452–7459.
(41) Kulshrestha, P.; Giese, R. F.; Aga, D. S. Investigating the molecular interactions of oxytetracycline in clay and organic matter: Insights on factors affecting its mobility in soil. *Environ. Sci. Technol.* **2004**, *38* (15), 4097–4105.
(42) Gao, J. A.; Pedersen, J. A. Adsorption of sulfonamide antimicrobial agents to clay minerals. *Environ. Sci. Technol.* **2005**, *39* (24), 9509–9516.
(43) Hamscher, G.; Pawelzick, H. T.; Hoper, H.; Nau, H. Different behavior of tetracyclines and sulfonamides in sandy soils after repeated fertilization with liquid manure. *Environ. Toxicol. Chem.* **2005**, *24* (4), 861–868.
(44) Blackwell, P. A.; Kay, P.; Boxall, A. B. A. The dissipation and transport of veterinary antibiotics in a sandy loam soil. *Chemosphere* **2007**, *67* (2), 292–299.
(45) Dolliver, H.; Gupta, S. Antibiotic losses in leaching and surface runoff from manure-amended agricultural land. *J. Environ. Qual.* **2008**, *37* (3), 1227–1237.
(46) Kay, P.; Blackwell, P. A.; Boxall, A. B. A. Fate of veterinary antibiotics in a macroporous tile drained clay soil. *Environ. Toxicol. Chem.* **2004**, *23* (5), 1136–1144.
(47) Carlson, J. C.; Mabury, S. A. Dissipation kinetics and mobility of chlortetracycline, tylosin, and monensin in an agricultural soil in Northumberland County, Ontario, Canada. *Environ. Toxicol. Chem.* **2006**, *25* (1), 1–10.
(48) De Liguoro, M.; Cibin, V.; Capolongo, F.; Halling-Sorensen, B.; Montesissa, C. Use of oxytetracycline and tylosin in intensive calf farming: evaluation of transfer to manure and soil. *Chemosphere* **2003**, *52* (1), 203–212.
(49) De Liguoro, M.; Poltronieri, C.; Capolongo, F.; Montesissa, C. Use of sulfadimethoxine in intensive calf farming: evaluation of transfer to stable manure and soil. *Chemosphere* **2007**, *68* (4), 671–676.
(50) Aust, M. O.; Godlinski, F.; Travis, G. R.; Hao, X. Y.; McAllister, T. A.; Leinweber, P.; Thiele-Bruhn, S. Distribution of sulfamethazine, chlortetracycline and tylosin in manure and soil of Canadian feedlots after subtherapeutic use in cattle. *Environ. Pollut.* **2008**, *156* (3), 1243–1251.
(51) Wang, C. P.; Ding, Y. J.; Teppen, B. J.; Boyd, S. A.; Song, C. Y.; Li, H. Role of Interlayer Hydration in Lincomycin Sorption by Smectite Clays. *Environ. Sci. Technol.* **2009**, *43* (16), 6171–6176.
(52) Kreuzig, R.; Holtge, S. Investigations on the fate of sulfadiazine in manured soil: Laboratory experiments and test plot studies. *Environ. Toxicol. Chem.* **2005**, *24* (4), 771–776.
(53) Wang, Q. Q.; Bradford, S. A.; Zheng, W.; Yates, S. R. Sulfadimethoxine degradation kinetics in manure as affected by initial concentration, moisture, and temperature. *J. Environ. Qual.* **2006**, *35* (6), 2162–2169.
(54) Singleton, M. J.; Esser, B. K.; Moran, J. E.; Hudson, G. B.; McNab, W. W.; Harter, T. Saturated zone denitrification: Potential for natural attenuation of nitrate contamination in shallow groundwater under dairy operations. *Environ. Sci. Technol.* **2007**, *41* (3), 759–765.
(55) Meyer, D.; Reed, B.; Batchelder, C.; Zallo, I.; Ristow, P. L.; Higginbotham, G.; Arana, M.; Shultz, T.; Mullinax, D. D.; Merriam, J. Water use and winter liquid storage needs at central valley dairy farms in California. *Appl. Eng. Agric.* **2006**, *22* (1), 121–126.

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